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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
09/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,011	NATUNEN ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *87-138* is/are pending in the application.

4a) Of the above claim(s) *87-131* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *132-138* is/are rejected.

7)☒ Claim(s) *133* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed June 16, 2008 in response to the Office Action of January 14, 2008 is acknowledged. Applicant elected with traverse Group X, claims 132-135.

2. Applicants argue that although Examiner has cited Hanisch et al, Applicants point out that this reference fails to disclose a structure related to cancer but rather describes a soluble mucin which does not have any significance related to the present invention describing the detection of saccharide structures on the surface of cancer tissues. Applicants argue that the present claims all share the same or corresponding special technical feature which represents a contribution over the prior art (p. 12).

The arguments have been considered but are not found persuasive because the technical feature linking the groups is a substance binding to a human oligosaccharide sequence containing a terminal protein linked GlcNAcβ-structure. Hanisch et al does teach a monoclonal antibody 2B5 that binds a human oligosaccharide sequence containing a terminal protein linked GlcNAcβ-structure and this structure is found in human gastric carcinoma as stated in the restriction requirement. Therefore, the prior art clearly teaches the general inventive concept. Thus, "special technical feature" does not define a contribution over the prior art. For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL.

3. Claims 87-138 are pending. Claims 136-138 are new. Claims 87-131 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 132-138 are currently being examined.

Claim Objections

4. Claim 133 is objected to because of the following informalities: The claim fails to end in a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 137 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 132-136 and 138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to a composition comprising **an enzyme substrate**, capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure of said surface for use as a medicine (claim 132), the composition according to claim 132, wherein said **enzyme substrate** is conjugated to an immunologically active substance and/or a toxic substance (claim 133), the composition according to claim 132, wherein said **enzyme substrate is a carbohydrate substance** capable of being transferred specifically to the surface of a pathogenic entity or malignant cell or tissue by the transferring enzyme (claim 134), the composition according to claim 132, wherein said transferring enzyme is a glycosyl transferase (claim 135), the composition according to claim 132, wherein said **enzyme substrate is a 2-modified monosaccharide residue** (claim 136), the composition according to claim 132, wherein said enzyme substrate is transferred by a galactosyltransferase which is engineered to transfer effectively 2-modified monosaccharides or by a natural GalNAc/GlcNAc-transferase with similar specificity with said modified galactosyltransferase from animals (claim 138).

The specification discloses enzyme substrates UDP-GalN-PEG-fluorescein (Figure 9) and UDP-GalN-biotin (Figure 5) which can be used to transfer labeled

galactosamine to acceptor terminal GlcNAc structures found on tumor cells in order to label tumor cells (Figure 10). The specification discloses radioactive labeled UDP-Gal as a substrate for galactosyltransferase to label muse teratocarcinoma cells (p. 5, lines 32-38). The specification discloses that modified monosaccharides to be used with glycosyltransferases are preferentially nucleotide sugar derivatives or analogs thereof, also other modified glycosides may be transferred by glycotransferases. Preferentially the nucleotide sugar or analog is a derivative of UDP-Gal or UDP-GalNAc where the toxic substance or immunologically active carbohydrate is linked to carbon number 2 or 6 of the Glc or GlcNAc residue or linked to a derivative or analog of GDP-Fuc or CMP-NeuNAc or CMP-sialic acid (p. 39, lines 10-25). The specification does not disclose any other **"enzyme substrates"** that are "capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure of said surface" or are a **"carbohydrate substance** capable of being transferred specifically to the surface of a pathogenic entity or malignant cell or tissue by the transferring enzyme" or a **"a 2-modified monosaccharide residue**" as broadly encompassed in the claims.

The art (see Bulter et al (Chemobiochem, 2001, 2:884-894)) teaches UDP-6-biotinyl-Gal or UDP-6-biotinyl-GalNAc, that is capable of being transferred by galactosyltransferase. US Patent Application Publication 2004/0253651 (Saarinen et al, published Dec. 2004, filed August 2002) teach enzyme substrate UDP-GalN that can be transferred to an acceptor non-reducing end terminal GlcNAc or glucose using a

glycosyltransferase ([0106]) or galactosyltransferase ([110]). However UDP-6-biotinyl-Gal, UDP-6-biotinyl-GalNA, UDP-GalN, or UDP-GalNAc do not provide an adequate representative number of species to support adequate written description for the broad genus of "enzyme substrates" as encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "enzyme substrates," "capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure of said surface," "carbohydrate substance capable of being transferred specifically to the surface of a pathogenic entity or malignant cell or tissue by the transferring enzyme" and "a 2-modified monosaccharide residue". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University

of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description the claimed enzyme substrate, per Lilly by structurally describing representative enzyme substrates or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe enzyme substrates useful in the claimed invention in a manner that satisfies either the Lilly or Enzo

standards. Although the specification discloses UDP-GalN-PEG-fluorescein, UDP-GalN-biotin, and UDP-GalN[-S-]-D structure, this does not provide a description of the broadly claimed enzyme substrates that would satisfy the standard set out in Enzo because the specification provides no structural features coupled to the functional characteristics.

Further, the specification also fails to describe enzyme substrates by the test set out in Lilly because the specification describes only UDP-GalN-PEG-fluorescein, UDP-GalN-biotin, and UDP-GalN[-S-]-D structure. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of an enzyme substrate that is required to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 132-136 and 138 are rejected under 35 U.S.C. 102(b) as being anticipated by Bulter et al (Chemobiochem, 2001, 2:884-894).

The claims are drawn to a composition comprising an enzyme substrate, capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure of said surface for use as a medicine (claim 132), the composition according to claim 132, wherein said enzyme substrate is conjugated to an immunologically active substance and/or a toxic substance (claim 133), the composition according to claim 132, wherein said enzyme substrate is a carbohydrate substance capable of being transferred specifically to the surface of a pathogenic entity or malignant cell or tissue by the transferring enzyme (claim 134), the composition according to claim 132, wherein said transferring enzyme is a glycosyl transferase enzyme (claim 135), wherein said enzyme substrate is a 2-modified monosaccharide residue (claim 136), the composition according to claim 132, wherein said enzyme substrate is transferred by a galactosyltransferase which is engineered to transfer effectively 2-modified monosaccharides or by a natural GalNAc/GlcNAc-transferase with similar specificity with said modified galactosyltransferase from animals (claim 138).

It is noted that the preamble recitation of "for use as a medicine" as recited in claim 132 is merely suggestive of an intended use and is not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredients *per se*, which is a composition comprising an enzyme substrate capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by

a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure (see MPEP 2111.02).

Bulter et al teach a composition comprising an enzyme substrate, UDP-6-biotinyl-Gal or UDP-6-biotinyl-GalNAc, that is capable of being transferred by galactosyltransferase (a glycosyl transferase) to acceptor structures such as BSA-$(GlcNAc)_{17}$ and ovalbumin, and is a carbohydrate substance and a 2-modified monosaccharide (abstract, p. 885; Scheme 1 and 2; Figures 3-7). Bulter et al teach the selective transfer of labeled nucleotide sugars onto specific acceptor structures in a glycoplipid or glycoprotein by glycosyltransferases, and teach that certain acceptor structures have tissue and cell-type specific expression associated with diseases such as cancer (p. 884, col. 1; p. 885, col. 1; p. 890, col. 1, paragraph 2; col. 2, last paragraph). Bulter et al teach the production of nonradioactive-labeled (fluorescein) or tagged (biotin) UDP-Gal and UDP-GalNAc for diagnostic applications (p. 885, col. 1). Biotin can elicit an immune response, hence would be an immunologically active substance.

The reference does not specifically teach that the labeled UDP-GalNAc or UDP-Gal is capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure, or transferred by a galactosyltransferase which is engineered to transfer effectively 2-modified monosaccharides or by a natural GalNAc/GlcNAc-transferase with similar specificity with said modified galactosyltransferase from animals, however, the claimed enzyme

substrate appears to be the same as the prior art enzyme substrate, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

8. Claims 132, 134-136, and 138 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication 2004/0253651 (Saarinen et al, published Dec. 2004, filed August 2002).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a composition comprising an enzyme substrate, capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure of said surface for use as a medicine (claim 132),

the composition according to claim 132, wherein said enzyme substrate is a carbohydrate substance capable of being transferred specifically to the surface of a pathogenic entity or malignant cell or tissue by the transferring enzyme (claim 134), the composition according to claim 132, wherein said transferring enzyme is a glycosyl transferase (claim 135), the composition according to claim 132, wherein said enzyme substrate is a 2-modified monosaccharide residue (claim 136), the composition according to claim 132, wherein said enzyme substrate is transferred by a galactosyltransferase which is engineered to transfer effectively 2-modified monosaccharides or by a natural GalNAc/GlcNAc-transferase with similar specificity with said modified galactosyltransferase from animals (claim 138).

It is noted that the preamble recitation of "for use as a medicine" as recited in claim 132 is merely suggestive of an intended use and is not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredients *per se*, which is a composition comprising an enzyme substrate capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure (see MPEP 2111.02).

Saarinen et al teach a composition comprising an enzyme substrate UDP-GalN that can be transferred to an acceptor non-reducing end terminal GlcNAc or glucose using a glycosyltransferase ([0106]) or galactosyltransferase ([110]). UDP-GalN is a carbohydrate substance.

The reference does not specifically teach that the UDP-GalN is capable of being transferred specifically to a surface of a pathogenic entity or malignant cell or tissue by a transferring enzyme making a covalent linkage between said enzyme substrate and an acceptor structure, 2-modified, or transferred by a galactosyltransferase which is engineered to transfer effectively 2-modified monosaccharides or by a natural GalNAc/GlcNAc-transferase with similar specificity with said modified galactosyltransferase from animals, however, the claimed enzyme substrate appears to be the same as the prior art enzyme substrate, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

9. **Conclusion:** No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Examiner, Art Unit 1642